John Wahren

Nicotine Physiology and Metabolism

Summary of current projects

1. The current status of knowledge regarding metabolism and pharmacokinetics of nicotine was updated and summarized at an international symposium in June 1992 at Salsomaggiore, Italy. The meeting was organized by Professors Gorrod and Wahren, who will also be the editors of the proceedings from the meeting. The publication will be a monograph entitled "Biochemistry and Metabolism of Nicotine and Related Alkaloids", published by Chapman and Hall Scientific Publishers, London. The work with the monograph is now in its final stages and publication is expected in July or August, 1993.

2. Studies are in progress concerning the influence of nicotine on regional circulation and metabolism of the human brain. They involve "functional imaging" of the brain by NMR-technique as well as determination of regional brain blood flow by PET-technique. The studies are being done in collaboration between the Karolinska Hospital, Stockholm and the Max-Planck Institute in Göttingen. The preliminary findings in three individuals receiving intravenous nicotine indicate that blood flow to the visual and auditory cortex is augmented by nicotine and, conversely, that flow to the cerebellum is diminished. The NMR- and PET-techniques lend themselves excellently to this type of study and the results may be the first demonstration of regional effects of nicotine on brain blood flow and metabolism in humans.

3. A study concerning hepatic and renal nicotine disposal in humans has been carried out together with Johan Gabrielsson. The results provide the first direct demonstration and quantitataive measurement of hepatic nicotine extraction in humans. The data were presented in preliminary form at the Salsomaggiore meeting and have now been evaluated and written up for a peer review journal. The final manuscript is now being adjusted and will be submitted within a month. It is a project that has received FTR support.

4. The effect of cigarette smoking on whole body energy expenditure on a short-term basis has been examined using indirect calorimetry. These studies extend previous findings concerning cigarette smoking and 24 h energy expenditure, published earlier by Hofstetter and Wahren in New England Journal of Medicine. The data describe the magnitude, time course and mechanism of nicotine's stimulatory action on energy expenditure. The study has been supported by FTR. A manuscript is under way and should be ready for submission by the end of June, 1993.

5. A study is in progress concerning the possible influence of liver disease on nicotine disposal. We have examined patients with cirrhosis of the liver during nicotine infusion. Additional studies are required, but the preliminary data indicate a delayed disposal of nicotine and a retarded conversion of nicotine to cotinine. A completed study should be ready within 4-6

2023251912

Source: https://www.industrydocuments.ucsf.edu/docs/jglm0000

months depending on the availability and outcome of the nicotine analyses.

6. A study has been undertaken to examine the relationship between arterial nicotine concentrations during cigarette smoking and nicotine content and puffing pattern. Thirty subjects participated in the study and a pneumotachograph was employed to determine the puff characteristics. The findings demonstrate large intra-individual variations in arterial nicotine concentration during smoking and that the cigarettes' nicotine yield or the smoking pattern both are of minor importance for the arterial nicotine concentration. The data have been evaluated and a preliminary manuscript is ready. The final paper will be sent for publication within 1-2 months.

Publications in progress

1. Biochemistry and metabolism of nicotine and related alkaloids, eds John Gorrod and John Wahren, Chapman and Hall, London, 1993 in press.

2. J Wahren. New methods for probing the *in vivo* disposition of nicotine in humans, in Biochemistry and metabolism of nicotine and related alkaloids, eds J Gorrod and J Wahren, Chapman and Hall, London, 1993 in press.

3, J Wahren, J Gabrielsson, M Curvall. Hepatic and renal exchange of nicotine in humans. J Clin Pharmacol Ther 1993, to be submitted.

4. J Wahren, Y Schutz, R Söderberg. Stimulation of energy expenditure during cigarette smoking. Am J Physiol 1993, to be submitted.

5. J Wahren, R Söderberg. Arterial nicotine and cotinine concentrations and cigarette smoking patterns. Clin Sci 1993, to be submitted.

2023251913

Source: https://www.industrydocuments.ucsf.edu/docs/jglm0000